REMARKS

Claims 12 and 28 have been amended to make more definite. Claim 25 has been amended in part to address the examiner's rejection and provide proper antecedent basis. Claim 26 has been amended to correct a typographical error. Applicants have added new claims 29 and 30 in order to rejoin restricted process claims support for which can be found in the specification, for example at paragraphs [0012], [0013], [0046] and Example 7. These new claims include all of the limitations of claim 24, which Examiner has indicated as allowed. It is believed that none of these amendments constitute new matter and their entry is requested.

Applicants appreciate the Examiner's time in the telephone conversation of November 27, 2007, in which this attorney for Applicants' outlined the proposed amendments to the specification and claims, as reflected in this Amendment and Response to Advisory Action. In that discussion the Examiner indicated that the amendments made herein would overcome the rejections of claims 12, 25 and 28, and the objections to the specification. Newly added claims 29 and 30 which rejoin restricted method claims, were discussed. However no decision was made as to the allowability of claims 29 and 30.

SPECIFICATION

Applicants have amended paragraphs [0002] and [0057] in order to correct administrative errors in the proper identification of government interest and cited references. Applicants have amended paragraph [0094] in order to comply with the provisions of 37 C.F.R. 1.809(d).

CLAIM OBJECTIONS

Claim 25 has been amended as required by the Examiner to further clarify that the DNA fragment is fused to the BCG hsp60 gene, and to provide proper antecedent basis for the promoter. Withdrawal of this objection is therefore requested.

35 USC § 112, second paragraph

Claims 12 and 28 have been rejected in the Office Action under 35 USC § 112, second paragraph, as being indefinite for failing to particularly print out and distinctly claim the subject matter of the invention.

Claim 12 has been rejected as indefinite for recitation of "genetic mycobacterium variants thereof". Applicant has amended claim 12 in order to clarify that it is naturally occurring or genetically modified mycobacterium of the listed strains, and any subspecies thereof, that are intended to be claimed.

Claim 28 has been rejected as indefinite for recitation of "producing a microorganism with an altered level of D-alanine ligase expression relative to a non-transformed microorganism." Claim 28 has been amended to clarify that it is the level of D-alanine ligase expression of the corresponding non-transformed microorganism that is intended to be claimed. Withdrawal of the rejections under 35 USC § 112, second paragraph are therefore requested.

35 USC § 112, first paragraph

Claims 24 and 25 have been rejected under 35 USC § 112, first paragraph, for lack of enablement. Applicants traverse the rejection of claim 24 and assert that the recombinant mycobacterium of claim 24 requires the use of biological materials that are capable of being prepared by one skilled in the art without undue experimentation from readily available starting materials using the description in the instant specification.

One skilled in the art could make and use mycobacterium strain GPM265 following repeatable methods set forth in the application (see Examples 1 and 2 and Table 1), using available starting materials - strain MC^2 155 is publicly available from ATCC (designated MC(2)155) (Exhibit 9) - and the pBUN276 plasmid is on deposit with ATCC and designated

PTA-8190. As such, no deposit is required (27 C.F.R. 1.802(b)). When an organism is created by insertion of genetic material into a cell obtained from generally available sources, all that is required is a description of the means of carrying out the invention. *Amgen*, 927 F.2d (a) 1211. That some experimentation is necessary does not constitute lack of enablement as long as it is not unduly extensive. *Atlas Powder Co. v. E. I. duPont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984).

Applicants further point out that the information on both the plasmid and GPM265 is described in the manuscript filed with the related provisional application (Feng and Barletta, 2003 Jan; *Antimicrobiol Agents and Chemotherapy*, 47(1):283-291). In order to publish in this journal, applicants were required to agree to distribute both the plasmid pMV262 and GPM265 to the public. As requested by the examiner, Applicant clarifies that ATCC deposit designated PTR-8190 does not contain GPM265.

Applicants have amended claim 25 to remove the requirement that the claimed plasmid specifically comprise *E.coli*-mycobacaterium shuttle vector be pMV262. Support for this amendment can be found in the instant specification, for example at paragraph [0080]. Applicants designed the construct of claim 25 that was used to generate a recombinant plasmid that expressed episomal *M. tuberculosis ddl* gene, specifically a *ddl* gene fragment was fused in frame with the first six codons of *M. bovis* BCG hsp60 and operably linked to the promoter of the-*M. bovis* BCG hsp60 gene, and a DNA fragment was cloned into an *E. coli* – mycobacterium shuttle vector. Therefore, withdrawal of the rejection is requested.

In view of the foregoing amendments and remarks, it is respectfully submitted that the claims now presented are patentable over the prior art of record and therefore in condition for allowance and eventual issuance. Such action is respectfully requested. Should the Examiner

have any further questions or comments which need be addressed in order to obtain allowance, please contact the undersigned attorney at the direct number listed below.

Respectfully submitted,

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